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EXAMINER
OLSON, ERIC

ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/621,027	CHEUNG, NAI-KONG V.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *193-238* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *193-238* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

This office action is a response to applicant's communication submitted June 4, 2007 wherein claims 149-192 are cancelled and new claims 193-238 are introduced. This application is a continuation in part of PCT/US02/01276, filed January 15, 2002, which claims benefit of 60/261911, filed January 16, 2001.

Claims 193-238 pending in this application.

Claims 193-238 as amended are examined on the merits herein.

Applicant's amendment, submitted May 22, 2007, with respect to the rejection of instant claims 149-192 under 35 USC 112, first paragraph for lacking enablement for a composition comprising any anticancer antibody whatsoever, has been fully considered and found to be persuasive to remove the rejection as the rejected claims are cancelled and the new claims are directed specifically to a complement-activating antibody that binds to a cancer cell. Therefore the rejection is withdrawn.

Applicant's amendment, submitted May 22, 2007, with respect to the rejection of instant claims 149-167 under 35 USC 101 for claiming the same invention as claims 89-107 of copending application 11/218044, has been fully considered and found to be persuasive to remove the rejection as the rejected claims are cancelled and the new claims are not identical to any claims of 11/218044. Therefore the rejection is withdrawn.

The following rejections of record in the previous office action are maintained:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 193-198, 208-224, and 228-238 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yan et al. (of record in previous office action) in view of Jamas et al. (US patent 5859720, of record in previous office action) Yan et al. discloses a method of producing a synergistic complement-mediated antitumor effect comprising administering a yeast-derived beta-glucan composition (denoted as SZP_g) to a mouse xenograft model of breast cancer (p. 304, right column) in combination with antitumor antibodies. (p. 3048, left column and figure 3) The beta-glucan has a 1,3-linked backbone and is branched with 1,6-linked side chains, (p. 3045, left column, first paragraph) and is obtained from yeast. (zymosan) The combination therapy led to a synergistic effect producing more than additive results in the mice. It is explained that the normal antitumor effects of beta-glucans is only present in specific strains of mice having appropriate antibodies toward the tumor, and that the addition of exogenous antitumor antibodies can restore this activity in cases in which beta-glucan monotherapy is ineffective. (p. 3050, under the heading **Discussion**) Anti-GD2 antibodies are cited as a specific example. (p. 3050, right column, first paragraph) Because the two elements of the therapy, namely the antibody and the glucan, were administered together to the

same subject, they are reasonably considered to be a "pharmaceutical combination" even if they were not physically combined before being administered to the subject. Furthermore, the beta-glucan compositions in phosphate-buffered saline described by Yan et al. and used for intravenous or intraperitoneal injection are also "orally administered " compositions because they are suitable fore being ingested orally. Yan et al. does not disclose a combination in which the beta-glucan has the specific molecular weights of claim 193, or the viscosities of claims 216-218 and 236-238, or in which it is present in a dosage of at least 25 mg/kg/day.

Jamas et al. discloses an orally administered immune-stimulating beta-glucan preparation, (column 4, lines 40-64) derived from yeast, bacteria, fungi, and plants. (column 1, lines 13-15) which has a molecular weight of 10000-500000 daltons, (column 4, lines 23-35) and is stable to heat treatment. (columns 5-6, examples 1-2) This beta-glucan has a 1,3-linked backbone and 1,6-linked branches, (column 4, lines 11-20) and is thus the same glucan described by Yan et al. The necessary dose varies on an individual basis. (column 4, lines 49-53) These glucans are useful either alone or as adjuvants to other therapies. (column 4, lines 26-29)

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the method of Yan et al. with a beta-glucan composition described by Jamas et al. comprising a beta-glucan with the molecular weight and heat stability of the claimed invention, and to administer the composition orally at a dosage of at least 25 mg/kg/day. One of ordinary skill in the art would have been motivated to use the composition of Jamas et al. because this composition contains a beta-glucan having the

same 1,3 and 1,6-linkages described by Yan et al. and to administer it orally because Jamas et al. discloses that the composition produces a systemic effect (immunostimulation) when administered orally. Note that the specific heat-stability of the claimed glucan is an inherent property of the claimed invention and is thus present in the composition of Jamas et al. because the beta-glucan molecule in this composition is the same as that of the claimed invention. One of ordinary skill in the art would reasonably have expected success in using the composition of Jamas et al. because this composition comprises a beta-glucan which has the same backbone and linkages as that used by Yan et al. One of ordinary skill in the art would have reasonably expected success in producing an appropriate pharmaceutical composition and administering the claimed dose because the preparation of pharmaceutical composition comprising known active ingredients and the selection of specific dosages of known medications is part of the ordinary and routine level of skill in the art.

As regards the range of viscosities disclosed in instant claims 216-218 and 236-238, any beta glucan can be prepared in an aqueous solution having the recited viscosities at room temperature or at physiological temperature by selecting an appropriate concentration. Such solutions are suitable for oral administration. One of ordinary skill in the art would, in the process of preparing the beta glucan for oral administration, test a wide range of possible concentrations of beta glucan to determine which is the optimal dosage form. This experimentation is merely routine and predictable.

Thus the invention taken as a whole is *prima facie* obvious.

Response to Argument: Applicant's arguments, filed May 22, 2007, with respect to the above rejection, have been fully considered and not found persuasive to remove the rejection. Applicant argues that oral administration produces unexpected results because orally administering the beta-glucan would not be expected to produce a systemic effect due to the supposed unpredictably of oral administration and the lack of understanding of oral administration at the time of the invention. However, the instant claims do not recite a method comprising orally administering a beta-glucan. They recite a combination of two compositions, one of which is an "orally administered" composition comprising a beta-glucan. Note that the intended use of a composition only limits the composition insomuch as the composition inherently **could** be used for the intended use. The fact that the composition is described by Yan et al. as being injected rather than orally ingested does not change the fact that it is suitable for oral administration as well. Thus, in this context, "orally administered" is interpreted to mean that the composition could be orally administered.

Additionally, even if the composition were to be interpreted as only being suitable for oral administration (e.g. a tablet) said composition would still be obvious over the recited references. Administering a pharmaceutical orally is routine and predictable. Thousands of pharmaceuticals are successfully administered by the oral route, indicating predictability of this delivery method. Furthermore, Jamas et al. specifically includes oral administration in a recitation of possible routes of administration by which the disclosed glucans can be administered to a patient. Contrary to Applicant's assertion, it would be highly unusual and unexpected if, in view of the fact that Jamas

does in fact teach that beta-glucans produce a systemic effect when administered orally, and are useful alone or as adjuvants to other therapies, these beta-glucans were to fail to demonstrate the antibody-enhancing effects described by Yan et al. when administered orally. In response to Applicant's statement that, "The crux of Examiner's rationale appears to be that Jamas's mere reference to orally administered glucan constitutes sufficient 'teaching' to provide a reasonable expectation of success in arriving at the claimed subject matter," this is indeed the case. It is in fact true that **any reference whatsoever in the prior art, particularly in an issued US patent, that indicates that a therapeutic agent can be administered orally to produce a systemic effect is sufficient teaching to provide a reasonable expectation of success in administering that agent orally**.

Furthermore, the references Harada et al., "Oral Administration of PSK can improve the Impaired Anti-Tumor CD4+ T-Cell Response in Gut-Associated Lymphoid Tissue (GALT) of Specific-Pathogen-Free Mice" Int. J. Cancer (1997) **70** 362-372; Nanba et al. "Effect of Maitake D-Fraction an Cancer Prevention" Ann. NY Acad. Sci. (1997) Vol. 833, pp. 204-207; Nanba et al. "Antitumor Action of Shiitake "*Lentinus edodes*) Fruit Bodies Orally Administered to Mice" Chem. Pharm. Bull. (1987) Vol 35, No. 6, pp. 2453-2358; Nanba et al. "Antitumor Mechanisms of Orally Administered Shitake fruit bodies" Chem. Pharm. Bull. (1987) Vol. 5, No. 6, pp. 2459-2464; indicate that orally administered beta-glucans were in fact known in the art to produce systemic immunostimulating effects.

Applicant further argues that the various prior art references to oral administration of beta-glucan do not concern the enhancement of exogenously administered antibodies. However, given that the prior art does disclose that orally administered beta glucan has a **systemic** immunostimulating effect, one of ordinary skill in the art would reasonably expect that the different systemic effect observed by Yan et al. would also be observed with orally administered beta glucan. There is no reason to believe based on the prior art that the orally administered beta glucan would possess the disclosed generic immunostimulatory effect but not the specific antibody-enhancing effect.

Applicant further argues that this rejection improperly regards the teaching of Yan in view of Jamas as a silver bullet for treating all types of cancers, in contradiction to the rejection under 35 USC 112, firs paragraph, of record in the previous office action. This is not true. The only type of cancer relied upon in the above rejection is breast cancer, in line with the use of the beta glucan and antibodies in Yan et al. to treat mammary carcinoma in mice. All of the rejected claims read on the treatment of breast cancer by this method.

Still further, Applicant argues that the claimed method of oral administration of lentanan produces an unexpectedly greater effect when compared to intraperitoneal administration of lentinan. However, according to MPEP 716.02(d), Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the "objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support." In

other words, the showing of unexpected results must be reviewed to see if the results occur over the entire claimed range. In re Clemens, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980) See also In re Peterson, 315 F.3d 1325, 1329-31, 65 USPQ2d 1379, 1382-85 (Fed. Cir. 2003); In re Grasselli, 713 F.2d 731, 741, 218USPQ 769, 777 (Fed. Cir. 1983) IN the instant case, Applicant provides a single figure comparing the oral and intraperitoneal administration of one particular lentinan. This lentinan is not considered to be representative of the full range of beta-glucans, having different molecular weights, branching patterns, biological sources, and other characteristics.

Finally, Applicant argues that persons with greater than ordinary skill in the art recognized the claimed method as a breakthrough. This is not relevant as such considerations cannot overcome the undisputed fact that before the filing date others in the art already knew that it was possible to produce a systemic immunostimulatory effect by orally administering beta glucan.

Finally, Applicant argues that the claimed invention meets the long-felt need for orally administrable cancer therapeutics, and gives as examples the problems associated with oral delivery of peptides and proteins, and chemotherapeutics. As the claimed therapeutic agent is not a peptide or protein, and differs significantly in both structure and mechanism of action from conventional cancer chemotherapeutics, these examples are not seen to be analogous to the instant case or to demonstrate that the "long felt need" in the art for orally bioavailable beta-glucan. Furthermore, there already existed multiple orally bioavailable beta-glucans at the time of the invention, for example

Jamas et al., Nanba et al., Harada et al., Suzuki et al., and Ohno et al. (References included with PTO-892)

Finally, Applicant asserts that beta glucans cannot traverse the lipophilic plasma membrane due to their content of hydroxyl groups. This argument is unpersuasive because, as discussed above, beta-glucans were known at the time of filing to be orally bioavailable. Clearly they do avoid the problem of intestinal absorption in one way or another.

For these reasons, the rejection is deemed proper and made **FINAL**.

Claims 200, 201, 207, 226, and 227 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yan et al. (of record in previous office action) in view of Jamas et al. (US patent 5859720, of record in previous office action) as applied to claims 108-112, 123-126, 130-142, and 146-156 above, and further in view of any one of Cheever et al., (US patent 6664370, Reference of record in previous action) Onizuka et al., (Reference of record in previous action) Herrera et al., (Reference of record in previous action) or Rai et al. (Reference of record in previous action) The disclosure of Yan et al. in view of Jamas et al. is described above. Yan et al. in view of Jamas et al. does not explicitly disclose a method or composition involving an antibody that recognizes any of the antigens CD20, CD22, Her-2/neu, or CD25.

Cheever et al. discloses that the Her-2/neu antigen is an oncogene which is overexpressed in a variety of cancers including breast, ovarian, colon, lung, and prostate. (column 2, lines 1-21) Cheever et al. also discloses that the immune system

mounts an autochthonous immune response against HER-2/neu expressed by tumors which can be used to diagnose, monitor, and treat malignancies which overexpress this protein. (column 8, line 57 – column 9, line 15)

Onizuka et al. discloses a method of treating cancer by administering an anti-CD25 monoclonal antibody. (p. 3128, left column, bottom paragraph)

Herrera et al. discloses a method of treating cancer comprising administering anti-CD22 antibodies. (p. 853, left column, last paragraph)

Rai et al. discloses an anti-CD20 monoclonal antibody referred to as rituximab, which exerts cell- and compliment- mediated cytotoxicity against tumor cells *in vivo*. (p. 139, right column, last paragraph – p. 14, left column, first paragraph)

It would have been obvious to one of ordinary skill in the art at the time of the invention to use any of the monoclonal antibodies disclosed by Cheever et al., Onizuka et al., Herrera et al., or Rai et al. in the methods and compositions of Yan et al. in view of Jamas et al. One of ordinary skill in the art would have been motivated to use these antibodies because Yan et al. already discloses that beta-glucan produces a synergistic antitumor effect *in vivo* when combined with antitumor antibodies. One of ordinary skill in the art would have reasonably expected success because the disclosed antibodies have already been shown to be effective *in vivo*.

Thus the invention taken as a whole is *prima facie* obvious.

Response to Argument: Applicant's arguments, filed May 22, 2007, with respect to the above rejection, have been fully considered and not found persuasive to remove the rejection. Applicant's arguments are the same as those presented above in the

previous rejection and are not found persuasive for the same reason. Therefore the rejection is deemed proper and made **FINAL**.

Applicant's amendment submitted June 4, 2007, necessitates the following new grounds of rejection:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 216-218 and 236-238 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are drawn to glucans having specific viscosities. They do not indicate what solvent, temperature, and concentration the viscosity is being measured in. Furthermore they do not clearly state whether the viscosity is an inherent property of the glucan (i.e. a glucan having X viscosity in aqueous solution at Y concentration at room temperature) or a property of the particular dosage form being administered, affected by such factors as concentration, temperature, and pharmaceutical additives. (i.e. a pharmaceutical composition comprising a beta-glucan, the pharmaceutical composition having viscosity X) Therefore one skilled in the art would have no idea how these limitations actually limit the subject matter, and the claims are indefinite. Because this rejection was necessitated by amendment, the rejection is made **FINAL**.

Claims 193-238 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are drawn to a "pharmaceutical combination" comprising a complement-activating antibody and a beta-glucan. It is not clear what a pharmaceutical combination is, or in what way the two components are combined. For example, the limitation could mean that the components are physically combined. Alternately it could mean that they are provided in a kit in which both components are packaged together, or it could merely mean that the two components are present in the same room, or that they are both described as useful for treating the same purpose. In the absence of any definition of a "pharmaceutical combination" in the specification, this term is considered to be indefinite. Because this rejection was necessitated by amendment, the rejection is made **FINAL**.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 216-218 and 236-238 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant's amendment submitted May 22, 2007 with respect to the aforementioned claims has been fully considered and but is deemed to insert **new matter** into the claims since the

specification as originally filed does not provide support for solutions of glucans having the specific recited viscosities of 5.6-100, 20-100, or 30-69 cst. As the instant specification as filed contains no description of these ranges the specification as originally filed does not provide support for the subject matter of instant claims 127-129 and 157-159. See *in re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972). Because this rejection was necessitated by amendment, the rejection is made **FINAL**.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 200, 202, 203, and 226 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yan et al. (of record in previous office action) in view of Jamas et al. (US patent 5859720, of record in previous office action) as applied to claims 108-112, 123-126, 130-142, and 146-156 above, and further in view of Maloney et al. (Reference of record in PTO-892) The disclosure of Yan et al. in view of Jamas et al. is discussed above. Yan et al. in view of Jamas et al. does not disclose a method wherein the antibody is directed to a cancer cell expressing the antigen CD20, or a cancer cell that is a non-Hodgkin's lymphoma.

Maloney et al. discloses a clinical trial of the chimeric anti-CD20 monoclonal antibody IDEC-C2B8 in patients suffering from relapsed (non-Hodgkin's) B-cell

lymphoma expressing the CD20 antigen. (p. 2189, left column, paragraphs 3-4) This therapy compares favorably in its effectiveness with other therapies in use for this condition. (p. 2193, left column, paragraph 2)

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the IDEC-C2B8 antibody in the method of Yan et al. in view of Jamas, and to use it in a patient suffering from non-Hodgkin's lymphoma. Because the antibody of Maloney et al. is an antitumor monoclonal antibody similar to those used by Yan et al., the substitution of one known monoclonal antibody for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Similarly, the substitution of a non-Hodgkin's lymphoma for the breast tumors taught by Yan et al. would be obvious because Maloney et al. discloses that the IDEC-C2B8 antibody is effective at treating this condition. The substitution of one element for another is a routine and predictable modification for one of ordinary skill in the art.

Thus the invention taken as a whole is *prima facie* obvious. Because this rejection was necessitated by amendment, the rejection is made **FINAL**.

Claim 205 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yan et al. (of record in previous office action) in view of Jamas et al. (US patent 5859720, of record in previous office action) as applied to claims 108-112, 123-126, 130-142, and 146-156 above, and further in view of Bergman et al. (Reference of record in PTO-892) The disclosure of Yan et al. in view of Jamas et al. is discussed above. Yan et al. in

view of Jamas et al. does not disclose a method wherein the antibody is directed to a cancer cell that is a neuroblastoma or melanoma.

Bergman et al. discloses a therapeutic method where the antibody 3F8, and anti-GD2 monoclonal antibody, is administered to rats bearing melanoma or neuroblastoma tumors. (p. 538, right column, second paragraph – p. 539, right column, fourth paragraph) The treatment prevented engraftment of the tumors and eradicated or retarded the growth of established tumors. (p. 542, left column)

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the 3F8 antibody in the method of Yan et al. in view of Jamas and to use it to treat neuroblastoma and melanoma. Because the antibody of Bergman et al. is an antitumor monoclonal antibody similar to those used by Yan et al., the substitution of one known monoclonal antibody for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Similarly, the substitution of a melanoma or neuroblastoma for the breast tumors taught by Yan et al. would be obvious because Bergman et al. discloses that the 3F8 antibody is effective at treating this condition. The substitution of one element for another is a routine and predictable modification for one of ordinary skill in the art.

Thus the invention taken as a whole is *prima facie* obvious. Because this rejection was necessitated by amendment, the rejection is made **FINAL**.

Claim 202 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yan et al. (of record in previous office action) in view of Jamas et al. (US patent 5859720, of

record in previous office action) as applied to claims 108-112, 123-126, 130-142, and 146-156 above, and further in view of Capurro et al. (Reference of record in PTO-892) The disclosure of Yan et al. in view of Jamas et al. is discussed above. Yan et al. in view of Jamas et al. does not disclose a method wherein the antibody is directed to a cancer cell that is a Hodgkin's lymphoma.

Capurro et al. discloses that the monoclonal antibody FC-2.15 is reactive against a wide range of neoplastic tissues in including Hodgkin's lymphoma. (p. 334, right column, first paragraph)

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the FC-2.15 antibody in the method of Yan et al. in view of Jamas and to use it to treat Hodgkin's lymphoma. Because the antibody of Capurro et al. is an antitumor monoclonal antibody similar to those used by Yan et al., the substitution of one known monoclonal antibody for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Similarly, the substitution of a Hodgkin's lymphoma for the breast tumors taught by Yan et al. would be obvious because Capurro et al. discloses that the FC-2.15 antibody is effective at treating this condition. The substitution of one element for another is a routine and predictable modification for one of ordinary skill in the art.

Thus the invention taken as a whole is *prima facie* obvious. Because this rejection was necessitated by amendment, the rejection is made **FINAL**.

Claims 199, 206, and 225 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yan et al. (of record in previous office action) in view of Jamas et al. (US patent 5859720, of record in previous office action) as applied to claims 108-112, 123-126, 130-142, and 146-156 above, and further in view of Capurro et al. (Reference of record in PTO-892) The disclosure of Yan et al. in view of Jamas et al. is discussed above. Yan et al. in view of Jamas et al. does not disclose a method wherein the antibody recognizes GD3 or is directed to a cancer cell that is a melanoma.

Soiffer et al. discloses that the monoclonal antibody R24, which is directed to the antigen GD3, has been used successfully to treat malignant melanoma. (p. 17, right column, paragraph 2)

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the R24 antibody in the method of Yan et al. in view of Jamas and to use it to treat melanoma. Because the antibody of Soiffer et al. is an antitumor monoclonal antibody similar to those used by Yan et al., the substitution of one known monoclonal antibody for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Similarly, the substitution of a melanoma for the breast tumors taught by Yan et al. would be obvious because Soiffer et al. discloses that the R24 antibody is effective at treating this condition. The substitution of one element for another is a routine and predictable modification for one of ordinary skill in the art.

Thus the invention taken as a whole is *prima facie* obvious. Because this rejection was necessitated by amendment, the rejection is made **FINAL**.

Claim 197 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yan et al. (of record in previous office action) in view of Jamas et al. (US patent 5859720, of record in previous office action) as applied to claims 108-112, 123-126, 130-142, and 146-156 above, and further in view of Ren et al. (Translation of abstract included with PTO-892) The disclosure of Yan et al. in view of Jamas et al. is discussed above. Yan et al. in view of Jamas et al. does not disclose a method wherein the antibody recognizes the EGFR antigen.

Ren et al. discloses an observation of complement-dependent cytotoxicity of the EGFR-directed monoclonal antibody egf/r3(IgG2a) against lung cancer cells. (abstract)

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the egf/r3(IgG2a) antibody in the method of Yan et al. in view of Jamas for treating EGFR-expressing lung cancer. Because the antibody of Ren et al. is an antitumor monoclonal antibody similar to those used by Yan et al., the substitution of one known monoclonal antibody for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. The substitution of one element for another is a routine and predictable modification for one of ordinary skill in the art.

Thus the invention taken as a whole is *prima facie* obvious. Because this rejection was necessitated by amendment, the rejection is made **FINAL**.

Claim 204 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yan et al. (of record in previous office action) in view of Jamas et al. (US patent 5859720, of record in previous office action) in view of Ren et al. (translation of abstract included with PTO-892) further in view of D'amico et al. (Reference included with PTO-892) The disclosure of Yan et al. in view of Jamas et al. in view of Ren et al. is discussed above. Yan et al. In view of Jamas et al. in view of Ren et al. does not disclose a method in which the cancer is epidermoid cancer.

Damico et al. discloses a survey of the prevalence of various biological markers in different lung cancers. (p. 884, table 3) 68% of squamous cell carcinomas (epidermoid carcinomas) are EGFR positive.

It would have been obvious to one of ordinary skill in the art at he time of the invention to use the method of Yan et al. in view of Jamas et al. in view of Ren et al. to treat EGFR positive squamous cell lung carcinomas. One of ordinary skill in the art would have been motivated to treat these particular cancers because Ren et al. already discloses the treatment of lung cancers generally, and because D'amico et al. discloses that a large number of squamous cell carcinomas bear the EGFR protein and are thus potential targets for the antibodies of Ren et al. One of ordinary skill in the art would reasonably have expected success because Ren et al. already discloses that the antibodies are useful for EGFR positive lung cancers generally.

Thus the invention taken as a whole is *prima facie* obvious. Because this rejection was necessitated by amendment, the rejection is made **FINAL**.

Claims 197 and 204 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yan et al. (of record in previous office action) in view of Jamas et al. (US patent 5859720, of record in previous office action) as applied to claims 108-112, 123-126, 130-142, and 146-156 above, and further in view of Mendelsohn et al. (Reference included with PTO-892) The disclosure of Yan et al. in view of Jamas et al. is discussed above. Yan et al. in view of Jamas et al. does not disclose a method wherein the antibody recognizes the EGFR antigen.

Mendelsohn et al. discloses a study of a panel of monoclonal antibodies against the epidermal growth factor receptor. (p. 307, first paragraph – p. 308, first paragraph) One particular monoclonal antibody was shown to have an inhibitory effect on several epidermoid carcinoma cell lines both in cell culture and in mouse xenografts. (p. 310, first paragraph and table II, p. 311, first paragraph)

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the monoclonal antibodies of Mendelsohn et al. in the method of Yan et al. in view of Jamas for treating EGFR-expressing epidermoid carcinoma. Because the antibody of Mendelsohn et al. is a monoclonal antibody similar to those used by Yan et al. that inhibits the proliferation of epidermoid carcinoma cells, the substitution of one known monoclonal antibody for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. The substitution of one element for another is a routine and predictable modification for one of ordinary skill in the art.

Thus the invention taken as a whole is *prima facie* obvious. Because this rejection was necessitated by amendment, the rejection is made **FINAL**.

Conclusion

No claims are allowed in this application. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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